

Application No. 10/527,559

Amendment And Response Pursuant To 37 C.F.R. §1.111

Applicant: Richard H. Ebright

Date submitted: January 21, 2009

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Amendments to the Claims:

This claim listing replaces all prior versions and listings of claims in the application. Please amend the claims as follows:

Claim 1. (Original). A method for identifying an agent that binds to a bacterial RNAP homologous RNA-exit-channel amino-acid sequence in a first entity, comprising the steps of: (a) preparing a reaction solution including the agent to be tested and a first entity including a bacterial RNAP homologous RNA-exit-channel amino-acid sequence; and (b) detecting at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to the homologous bacterial RNAP RNA-exit-channel amino-acid sequence.

Claim 2. (Original). The method of claim 1 wherein the first entity is an intact bacterial RNAP.

Claim 3. (Original). The method of claim 1 wherein the first entity is a fragment of a bacterial RNAP.

Claim 4. (Currently amended). The method of claim 1 wherein the first entity is *Escherichia coli* RNAP ~~or a derivative thereof~~.

Claim 5. (Currently amended). The method of claim 1 wherein the first entity is *Bacillus subtilis* RNAP ~~or a derivative thereof~~.

Claim 6. (Original). The method of claim 1 further comprising the step of: detecting at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to a second entity that contains a derivative of a bacterial RNAP homologous RNA-exit-channel amino-acid sequence having at least one substitution, insertion, or deletion.

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Claim 7. (Original). The method of claim 6 wherein the second entity is a derivative of an intact bacterial RNAP.

Claim 8. (Original). The method of claim 6 wherein the second entity is a derivative of a fragment of a bacterial RNAP.

Claim 9. (Original). The method of claim 6 wherein the second entity is a derivative of *Escherichia coli* RNAP.

Claim 10. (Original). The method of claim 6 wherein the second entity is a derivative of *Bacillus subtilis* RNAP.

Claim 11. (Currently amended). The method of claim 1 further comprising comparison of: (a) at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to the first entity, and (b) at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to a eukaryotic RNAP-derivative.

Claim 12. (Currently amended). The method of claim 11 wherein the eukaryotic RNAP derivative is a human RNAP-derivative.

Claim 13. (Currently amended). The method of claim 11 wherein the eukaryotic RNAP derivative is a human RNAP II-derivative.

Claim 14. (Withdrawn). A method for identifying an agent that inhibits an activity of a bacterial RNAP by binding to a bacterial RNAP homologous RNA-exit-channel amino-acid

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sequence, comprising: (a) preparing a reaction solution comprising the agent to be tested and a first entity containing a bacterial RNAP homologous RNA-exit-channel amino-acid sequence; and (b) detecting at least one of the presence, extent, concentration-dependence, or kinetics of inhibition of an activity of said first entity, wherein inhibition involves binding of the agent to the homologous bacterial RNAP RNA-exit-channel amino-acid sequence.

Claim 15. (Withdrawn). The method of claim 14 wherein the first entity is an intact bacterial RNAP.

Claim 16. (Withdrawn). The method of claim 14 wherein the first entity is a fragment of a bacterial RNAP.

Claim 17. (Withdrawn). The method of claim 14 wherein first entity is *Escherichia coli* RNAP or a derivative thereof.

Claim 18. (Withdrawn). The method of claim 14 wherein the first entity is *Bacillus subtilis* RNAP or a derivative thereof.

Claim 19. (Withdrawn). The method of claim 14 wherein the activity is transcription initiation.

Claim 20. (Withdrawn). The method of claim 14 wherein the activity is transcription elongation.

Claim 21. (Withdrawn). The method of claim 14 wherein the activity is σ binding.

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Claim 22. (Withdrawn). The method of claim 14 wherein the activity is NTP binding.

Claim 23. (Withdrawn). The method of claim 14 wherein the activity is DNA binding.

Claim 24. (Withdrawn). The method of claim 14 wherein the activity is RNA binding.

Claim 25. (Withdrawn). The method of claim 14 wherein the activity is open-complex formation.

Claim 26. (Withdrawn). The method of claim 14 wherein the activity is RNA synthesis.

Claim 27. (Withdrawn). The method of claim 14 further comprising the step of: detecting at least one of the presence, extent, concentration-dependence, or kinetics of the inhibition by the agent of the activity of a second entity that contains a derivative of a bacterial RNAP homologous RNA-exit-channel amino-acid sequence having at least one substitution, insertion, or deletion.

Claim 28. (Withdrawn). The method of claim 27 wherein the second entity is a derivative of an intact bacterial RNAP.

Claim 29. (Withdrawn). The method of claim 27 wherein the second entity is a derivative of a fragment of a bacterial RNAP.

Claim 30. (Withdrawn). The method of claim 27 wherein the second entity is *Escherichia coli* RNAP or a derivative thereof.

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Claim 31. (Withdrawn). The method of claim 27 wherein the second entity is *Bacillus subtilis* RNAP or a derivative thereof.

Claim 32. (Withdrawn). The method of claim 27 wherein the activity is transcription initiation.

Claim 33. (Withdrawn). The method of claim 27 wherein the activity is transcription elongation.

Claim 34. (Withdrawn). The method of claim 27 wherein the activity is open-complex formation.

Claim 35. (Withdrawn). The method of claim 27 wherein the activity is NTP binding.

Claim 36. (Withdrawn). The method of claim 27 wherein the activity is DNA binding.

Claim 37. (Withdrawn). The method of claim 27 wherein the activity is RNA binding.

Claim 38. (Withdrawn). The method of claim 27 wherein the activity is open-complex formation.

Claim 39. (Withdrawn). The method of claim 27 wherein the activity is Gre-RNA synthesis.

Claim 40. (Withdrawn). The method of claim 27 wherein inhibition of an activity of the first entity and inhibition of an activity of the second entity are assessed sequentially.

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Claim 41. (Withdrawn). The method of claim 27 wherein inhibition of an activity of the first entity and inhibition of an activity of the second entity are assessed simultaneously.

Claim 42. (Withdrawn). The method of claim 14 further comprising comparison of: (a) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of the first entity, and (b) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of a eukaryotic RNAP derivative.

Claim 43. (Withdrawn). The method of claim 42 wherein the eukaryotic RNAP derivative is a human RNAP derivative.

Claim 44. (Withdrawn). The method of claim 42 wherein the eukaryotic RNAP derivative is a human RNAP II derivative.

Claim 45. (Withdrawn). The method of claim 14 wherein at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of the first entity also is compared to at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by an inhibitory compound specific to the bacterial RNAP homologous RNA-exit-channel amino-acid sequence of an activity of the first entity.

Claim 46. (Withdrawn). A method for identifying an agent that binds to a bacterial RNAP homologous RNA-exit-channel amino-acid sequence, comprising (a) preparing a reaction solution comprising the agent to be tested, a first entity containing a bacterial RNAP

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homologous RNA-exit-channel amino-acid sequence, and containing a detectable group within σ region 3.2; and (b) detecting a change in a property of the detectable group within σ region 3.2.

Claim 47. (Withdrawn). The method of claim 46 wherein the first entity is an intact bacterial RNAP.

Claim 48. (Withdrawn). The method of claim 46 wherein the first entity is a fragment of a bacterial RNAP.

Claim 49. (Withdrawn). The method of claim 46 wherein the first entity is *Escherichia coli* RNAP or a derivative thereof.

Claim 50. (Withdrawn). The method of claim 46 wherein the first entity is *Bacillus subtilis* RNAP or a derivative thereof.

Claim 51. (Withdrawn). The method of claim 46 wherein the reference compound contains a chromophore.

Claim 52. (Withdrawn). The method of claim 46 wherein the detectable group contains a fluorophore.

Claim 53. (Withdrawn). The method of claim 46 further comprising measurement of FRET.

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Claim 54. (Withdrawn). The method of claim 46 further comprising the step of: detecting at least one of the presence, extent, concentration-dependence, or kinetics of the binding of the agent to a second entity that contains a derivative of a bacterial RNAP homologous RNA-exit-channel amino-acid sequence having at least one substitution, insertion, or deletion.

Claim 55. (Withdrawn). The method of claim 54 wherein the second entity is a derivative of an intact bacterial RNAP.

Claim 56. (Withdrawn). The method of claim 54 wherein the second entity is a derivative of a fragment of a bacterial RNAP.

Claim 57. (Withdrawn). The method of claim 54 wherein the second entity is *Escherichia coli* RNAP or a derivative thereof.

Claim 58. (Withdrawn). The method of claim 54 wherein the second entity is *Bacillus subtilis* RNAP or a derivative thereof.

Claim 59. (Withdrawn). The method of claim 46 further comprising comparison of: (a) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of the first entity, and (b) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of a eukaryotic RNAP derivative.

Claim 60. (Withdrawn). The method of claim 59 wherein the eukaryotic RNAP derivative is a human RNAP derivative.

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Claim **61.** (Withdrawn). The method of claim 59 wherein the eukaryotic RNAP derivative is a human RNAP II derivative.

Claim **62.** (Withdrawn). A method for identifying an agent that binds to a bacterial RNAP homologous RNA-exit-channel amino-acid sequence, comprising (a) preparing a reaction solution comprising the agent to be tested, a reference compound that binds to a homologous bacterial RNAP RNA-exit-channel amino-acid sequence, and a first entity containing a bacterial RNAP homologous RNA-exit-channel amino-acid sequence, and (b) detecting at least one of the presence, extent, concentration-dependence, or kinetics of competition by the agent for binding of the reference compound to the homologous RNA-exit-channel amino-acid sequence.

Claim **63.** (Withdrawn). The method of claim 62 wherein the first entity is an intact bacterial RNAP.

Claim **64.** (Withdrawn). The method of claim 62 wherein the first entity is a fragment of a bacterial RNAP.

Claim **65.** (Withdrawn). The method of claim 62 wherein the first entity is *Escherichia coli* RNAP or a derivative thereof.

Claim **66.** (Withdrawn). The method of claim 62 wherein the first entity is *Bacillus subtilis* RNAP or a derivative thereof.

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Claim 67. (Withdrawn). The method of claim 62 wherein the reference compound contains a detectable group.

Claim 68. (Withdrawn). The method of claim 62 wherein the detectable group contains a chromophore.

Claim 69. (Withdrawn). The method of claim 62 wherein the detectable group contains a fluorophore.

Claim 70. (Withdrawn). The method of claim 62 wherein the reference compound is a chromophore-labeled inhibitory compound specific to the bacterial RNAP homologous RNA-exit-channel amino-acid sequence.

Claim 71. (Withdrawn). The method of claim 62 wherein the reference compound is a fluorophore-labeled inhibitory compound specific to the bacterial RNAP homologous RNA-exit-channel amino-acid sequence.

Claim 72. (Withdrawn). The method of claim 62 further comprising measurement of FRET.

Claim 73. (Withdrawn). The method of claim 62 further comprising the step of: detecting at least one of the presence, extent, concentration-dependence, or kinetics of the binding of the agent to a second entity that contains a derivative of a bacterial RNAP homologous RNA-exit-channel amino-acid sequence having at least one substitution, insertion, or deletion.

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Claim 74. (Withdrawn). The method of claim 73 wherein the second entity is a derivative of an intact bacterial RNAP.

Claim 75. (Withdrawn). The method of claim 73 wherein the second entity is a derivative of a fragment of a bacterial RNAP.

Claim 76. (Withdrawn). The method of claim 73 wherein the second entity is *Escherichia coli* RNAP or a derivative thereof.

Claim 77. (Withdrawn). The method of claim 73 wherein the second entity is *Bacillus subtilis* RNAP or a derivative thereof.

Claim 78. (Withdrawn). The method of claim 62 further comprising comparison of: (a) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of the first entity, and (b) at least one of the presence, extent, concentration-dependence, or kinetics of inhibition by the agent of an activity of a eukaryotic RNAP derivative.

Claim 79. (Withdrawn). The method of claim 78 wherein the eukaryotic RNAP derivative is a human RNAP derivative.

Claim 80. (Withdrawn). The method of claim 78 wherein the eukaryotic RNAP derivative is a human RNAP II derivative.

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Claim **81**. (Withdrawn). The method of claim 62 wherein at least one of the presence, extent, concentration-dependence, or kinetics of binding of the agent to the first entity is compared to at least one of the presence, extent, concentration-dependence, or kinetics of binding of an inhibitory compound specific to the bacterial RNAP homologous RNA-exit-channel amino-acid sequence to the first entity.